

**WHAT IS CLAIMED:**

1. A method of detecting a neurodegenerative disease in a mammal comprising:
  - 5 activating brain tissue of the mammal by application of radiation under conditions effective to promote a simultaneous multiphoton excitation of the brain tissue and to emit a fluorescence characteristic;
  - comparing the fluorescence characteristic to a standard fluorescence emitted by exciting healthy brain tissue of the mammal under the same conditions
  - 10 used to carryout said activating; and
  - identifying the brain tissue where the fluorescence characteristic differs from the standard fluorescence as potentially having a neurodegenerative disease.
2. The method according to claim 1 further comprising:
  - 15 treating the brain tissue with at least one photo-active agent prior to said activating.
3. The method according to claim 2, wherein the standard fluorescence is determined prior to said treating the brain tissue with at least one photo-active agent.
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4. The method according to claim 2, wherein the photo-active agent fluoresces upon binding to lesions of neurodegenerative disease or other neuroanomalies.
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5. The method according to claim 1, wherein the radiation is generated by a laser.
6. The method according to claim 1, wherein the radiation is  
30 pulsed.

7. The method according to claim 6, wherein the radiation is pulsed at a pulse width between about  $10^{-9}$  to  $10^{-15}$  second.

5 8. The method according to claim 5, wherein the laser is a mode-locked laser.

9. The method according to claim 1 further comprising: collecting radiation applied to the brain tissue.

10 10. The method according to claim 1, wherein the neurodegenerative disease is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, and Lou Gehrig's Disease.

15 11. The method according to claim 10, wherein the neurodegenerative disease is Alzheimer's Disease.

12. The method according to claim 11, wherein amyloid plaques are detected in the brain of the mammal.

20 13. The method according to claim 11, wherein neurofibrillary tangles are detected in the brain of the mammal.

25 14. The method according to claim 1, wherein the method is carried out *in vivo*.

15. The method according to claim 1, wherein said activating is carried out by passing the radiation through the skull of the mammal.

30 16. The method according to claim 15, wherein the radiation is passed through a portion of the skull of the mammal which has been thinned.

17. The method according to claim 1, wherein said activating is carried out by passing the radiation through the brain of the mammal with its skull opened.

18. The method according to claim 1, wherein the fluorescence  
5 characteristic is an autofluorescence characteristic.

19. A method of producing an image of brain tissue from a mammal comprising:

activating brain tissue of a mammal with radiation applied under  
10 conditions effective to promote a simultaneous multiphoton excitation of the brain tissue and to produce a fluorescence and

collecting the fluorescence to produce an image of the brain tissue.

20. The method according to claim 19 further comprising:  
15 treating the brain tissue with at least one photo-active agent prior to said activating.

21. The method according to claim 19, wherein the radiation is generated by a laser.  
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22. The method according to claim 19, wherein the radiation is pulsed.

23. The method according to claim 22, wherein the radiation is  
25 pulsed at a pulse width between about  $10^{-9}$  to  $10^{-15}$  second.

24. The method according to claim 21, wherein the laser is a mode-locked laser.

25. The method according to claim 19, wherein the brain tissue  
30 being imaged is affected with a neurodegenerative disease.

26. The method according to claim 25, wherein the neurodegenerative disease is selected from the group consisting of Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, and Lou Gehrig's Disease.

5 27. The method according to claim 26, wherein the neurodegenerative disease is Alzheimer's Disease.

28. The method according to claim 27, wherein amyloid plaques are imaged in the brain of the mammal.

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29. The method according to claim 27, wherein neurofibrillary tangles are detected in the brain of the mammal.

15 30. The method according to claim 19, wherein the method is carried out *in vivo*.

31. The method according to claim 19, wherein said activating is carried out by passing the radiation through the skull of the mammal.

20 32. The method according to claim 31, wherein the radiation is passed through a portion of the skull of the mammal which has been thinned.

25 33. The method according to claim 19, wherein said activating is carried out by passing the radiation through the brain of the mammal with its skull opened.

34. The method according to claim 19, wherein the fluorescence is autofluorescence.